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Study of Visometric Behavior of Complexes of Diltiazem with Cu(II) and Cr(III) in Non- Aqueous Solvent

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Abstract: Hypertension is the name of a condition in which blood pressure stays high for a long period of time. Blood pressure is a measure of the pressure of the blood against the blood vessel walls. Antihypertensive are medicines that help to lower blood pressure. Diltiazem is an important coronary vasodilator drug of the calcium channel blocker type. Diltiazem is primarily prescribed to treat hypertension, to decrease heart attack risk after coronary bypass surgery, for prevention of migraine, for treatment of protein excretion in urine and to prevent blockage in heart after transplantation. The viscometricbehaviour of complexes of diltiazem with Cu(II) and Cr(III) in non-aqueous solvent of varying composition have been determined. The viscosity pattern for both complexes show increase with increasing complex concentration and then decreases after Critical Micelles Concentration (CMC). The value of CMC is higher if the percentage of non-aqueous solvent is higher. Also the CMC of copper- diltiazemcomplex(CuDC) is lower than chromium- diltiazem complex(CrDC).

I. INTRODUCTION

Hypertension or high blood pressure is a cardiac chronic medical condition in which the systematic arterial blood pressure is elevated. Persistent hypertension is one of the risk factors for stroke, myocardial infraction, heart failure and is a leading cause of chronic kidney failure. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of associated health complications, although drug treatment may prove necessary in patients for whom lifestyle changes prove ineffective or insufficient. The risks associated with a given blood pressure are dependent upon the combination of risk factors in the specific individual. These include age, gender, ethnic origin, diet, smoking, family history, blood cholesterol and pre existing vascular diseases etc.

The degree to which hypertension can be prevented (1-2) depends on a number of features including current blood pressure level, sodium/potassium balance, detection and omission of environmental toxins, changes in target organs, risk factors for cardiovascular diseases and the age at diagnosis of hypertension. Following lifestyle changes are recommended to lower blood pressure, before the initiation of prescription drug therapy.

A. Weight reduction and regular aerobic exercise improves blood flow and helps to reduce blood pressure.
B. Reducing dietary sugar.
C. Reducing sodium in the body.
D. Additional dietary changes beneficial to reducing blood pressure include the DASH diet (Dietary Approaches to Stop Hypertension) which is rich in fruits and vegetables and low fat or fat-free dairy products.
E. Discontinuing tobacco use and alcohol has shown to lower blood pressure
F. Reducing stress. The first line of treatment for hypertension is the same as the recommended preventive lifestyle changes. If the hypertension is high enough to justify immediate use of medications, lifestyle changes are still recommended in conjugation with medication.Several classes of medications, collectively referred to as antihypertensive drugs (3-5) are currently available for treating hypertension. Agents within a particular class generally share a similar pharmacological mechanism of action and in many cases have an affinity for similar cellular receptors. Diltiazem (6) belongs to the group of drugs known as benzothiazepines, which are a class of calcium channel blockers, used in the treatment of hypertension, angina pectoris and some types of arrhythmia. Diltiazem is an important coronary vasodilator drug of calcium channel blocker type. Chemically, diltiazemHCl is (+)-cis 1,5-benzothiazepin-4-(5H) one,3-(acetoxy)-5-[2-(dimethylamino) ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-monohydrochloride.

II. EXPERIMENTAL

A. Preparation of Solutions

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1) *Preparation of solvent system:* Two types of solvent systems were prepared having aqueous: non- aqueous solvent ratio 80:20 and 60:40
2) *Drug solution preparation:* Diltiazemdilzem FR having 20 mg of content of drug in one tablet was used. The standard stock solution of drug was prepared by dissolving one crushed tablet in 100 ml solvent system
3) *Metal solution preparation:* High grade purity metal compound copper chloride and chromium chloride were used for the preparation of standard solution of metal. Calculated amount of metal compound was weighed and dissolved in 100 ml of solvent system
4) *Preparation of complex solution:* Complexes were prepared by mixing drug and metal solution in definite ratio.

B. Measurement of Viscosity and Specific Viscosity

Flowing is one of the most important characteristic properties of liquids. The rate of flow depends upon the nature of the liquid and on the force which produces the flow. Ostwald's Viscometer was used for measuring the viscosity of the complex solution .From the viscosity, the specific viscosity is measured. Solutions having different concentration of complex were prepared by dilution of standard stock solution.

III. RESULTS AND DISCUSSION

Flow characterization of solution of complexes in terms of viscometric measurements has been employed as a tool to find out CMC of complexes of diltiazem with copper and chromium.

The viscosity 'η' of the complexes of diltiazem with Cu(II) and Cr(III) in non-aqueous solvent of varying composition has been determined and recorded in Table-1 and Table-2 respectively. The viscosity for both the complexes was found to increase with the increase in complex concentration and then decreases or the increase in value is very small after a definite concentration corresponding to the CMC of the complexes. The increase in viscosity with the increase in concentration of complex solutions may be due to the increasing tendency of complex molecules to associate in the form of micelles. After CMC viscosity increases rapidly with increase in concentration of complex solutions.

The plots of viscosity η' against complex concentration, C(g mol^{-1}) are shown in Figure1 and Figure2 for Cu(II) and Cr(III) complexes respectively. The plots are characterized by an interaction of straight line and a convex curve with respect to X-axis at a definite concentration corresponding to CMC of complexes. The values of CMC in the higher volume percent of non-aqueous solvent is lower than that of lower volume percent of non-aqueous solvent. It is suggested that non-aqueous solvent take different position in the micelles and the complex exhibits different degree of aggregation in the mixed solvent of varying compositions. The value of CMC is in close agreement with those obtained from other physical properties and follow the order CrDC > CuDC.

The CMC of CrDC is higher because the average molecular weight of CrDC is lower than CuDC. Thus CMC value decreases with an increase in the molecular weight of the complex. This may be due to increase in the size of the micelles with the increase in the molecular weight. The value of specific viscosity, η_{sp} of CuDC and CrDC in 20% and 40% non-aqueous mixture are recorded in Table-3 and Table-4 respectively. The results show that specific viscosity of CuDC and CrDC initially increases with increase in complex concentration and then decreases which corresponds to the CMC of the complexes. This increase may be due to the increasing tendency of the complex solution molecules to form aggregates with increasing complex concentration. The value of CMC so obtained is in good agreement with the value obtained from the plot of viscosity against concentration of the complex.

IV. CONCLUSIONS

Viscometricbehaviour of metal complexes of Cu(II) and Cr(III) with diltiazem have been studied in non-aqueous solvent of varying composition. The viscosity for both complexes show increase with increasing complex concentration and then decreases at CMC. The value of CMC is lower if the percentage of non-aqueous solvent is higher. Also the CMC of CrDC is higher thanCuDC. Similar results are obtained on measurement of specific viscosity. The vlue of CMC in both the measurements are very near to each other.

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TABLE-1 VISCOSITY MEASUREMENT OF COPPER(II)-DILTIAZEM COMPLEX

Sr. No.	Concentration of Complex (g mol L^{-1})	Viscosity (mili poise) Volume% of non-aqueous in solvent mixture 20%	40%
1	$0.00x10^{-3}$	0.8249	0.9988
2	$0.50x10^{-3}$	1.3205	1.2893
3	$0.75x10^{-3}$	1.4742	1.3734
4	$1.00x10^{-3}$	1.5761	1.4637
5	$1.25x10^{-3}$	1.7587	1.5099
6	$1.50x10^{-3}$	1.8784	1.6094
7	$1.75x10^{-3}$	1.9067	1.6570
8	$2.00x10^{-3}$	1.9598	1.6532
9	$2.25x10^{-3}$	1.9645	1.6861
10	$2.50x10^{-3}$	1.9722	1.6431
11	$2.75x10^{-3}$	1.9858	1.6081
12	$3.00x10^{-3}$	2.0127	1.5698
13	$3.25x10^{-3}$	2.1082	1.8261
14	$3.50x10^{-3}$	2.2661	2.0744
15	$3.75x10^{-3}$	2.3492	2.3590
16	$4.00x10^{-3}$	2.4091	2.4704

TABLE-2VISCOSITY MEASUREMENT OF CHROMIUM(III)-DILTIAZEM COMPLEX

Sr. No.	Concentration of Complex(g mol L^{-1})	Viscosity (mili poise) Volume% of non-aqueous in solvent mixture 20%	40%
1	$0.00x10^{-3}$	0.8249	0.9988
2	$0.50x10^{-3}$	0.8952	1.0952
3	$0.75x10^{-3}$	1.0053	1.1567
4	$1.00x10^{-3}$	1.1857	1.4861
5	$1.25x10^{-3}$	1.4065	1.5549
6	$1.50x10^{-3}$	1.4943	1.6082
7	$1.75x10^{-3}$	1.5884	1.8556
8	$2.00x10^{-3}$	1.6534	2.0479
9	$2.25x10^{-3}$	1.7592	2.1852
10	$2.50x10^{-3}$	1.8008	2.3734
11	$2.75x10^{-3}$	1.7985	2.4915
12	$3.00x10^{-3}$	1.7765	2.5124
13	$3.25x10^{-3}$	1.6285	2.5641
14	$3.50x10^{-3}$	1.4715	2.6127
15	$3.75x10^{-3}$	1.4531	2.8675
16	$4.00x10^{-3}$	1.6472	3.1722

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r. No.	Concentration of Complex(g mol L^{-1})	Specific Viscosity (η_{sp}) Volume% of non-aqueous in solvent mixture	
		20%	40%
1	$0.00x10^{-3}$	–	–
2	$0.50x10^{-3}$	0.0112	0.1542
3	$0.75x10^{-3}$	0.0316	0.2652
4	$1.00x10^{-3}$	0.0831	0.3206
5	$1.25x10^{-3}$	0.1703	0.3375
6	$1.50x10^{-3}$	0.2112	0.3521
7	$1.75x10^{-3}$	0.2652	0.3727
8	$2.00x10^{-3}$	0.2681	0.3168
9	$2.25x10^{-3}$	0.2453	0.2328
10	$2.50x10^{-3}$	0.2381	0.1898
11	$2.75x10^{-3}$	0.1942	0.0939
12	$3.00x10^{-3}$	0.1594	0.0652
13	$3.25x10^{-3}$	0.1139	0.0842
14	$3.50x10^{-3}$	0.0928	0.1095
15	$3.75x10^{-3}$	0.0753	0.2698
16	$4.00x10^{-3}$	0.1681	0.3142

TABLE-3
SPECIFIC VISCOSITY MEASUREMENT OF COPPER(II)-DILTIAZEM COMPLEX

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TABLE-4
SPECIFIC VISCOSITY MEASUREMENT OF CHROMIUM(III)-DILTIAZEM COMPLEX

Sr. No.	Concentration of Complex(g mol L^{-1})	Specific Viscosity (η_{sp}) Volume% of non-aqueous in solvent mixture	
		20%	40%
1	$0.00x10^{-3}$	–	–
2	$0.50x10^{-3}$	0.0852	0.0965
3	$0.75x10^{-3}$	0.0985	0.1132
4	$1.00x10^{-3}$	0.0931	0.1354
5	$1.25x10^{-3}$	0.1085	0.1698
6	$1.50x10^{-3}$	0.1574	0.2347
7	$1.75x10^{-3}$	0.1758	0.2982
8	$2.00x10^{-3}$	0.1964	0.3292
9	$2.25x10^{-3}$	0.2055	0.3856
10	$2.50x10^{-3}$	0.2194	0.2224
11	$2.75x10^{-3}$	0.2349	0.2007
12	$3.00x10^{-3}$	0.2276	0.1768
13	$3.25x10^{-3}$	0.1573	0.0784
14	$3.50x10^{-3}$	0.0946	0.0548
15	$3.75x10^{-3}$	0.0122	0.0687
16	$4.00x10^{-3}$	0.0542	0.0944

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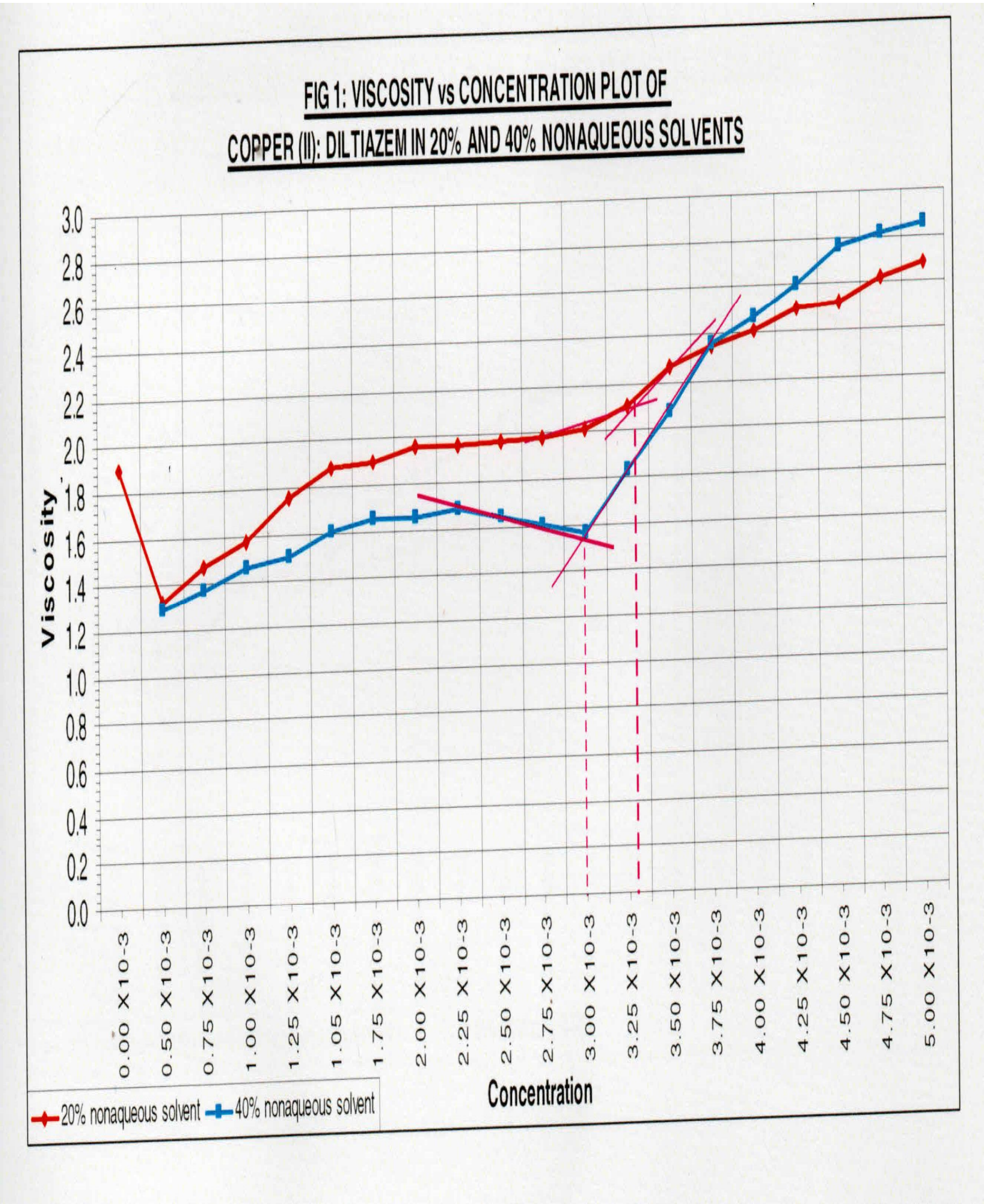

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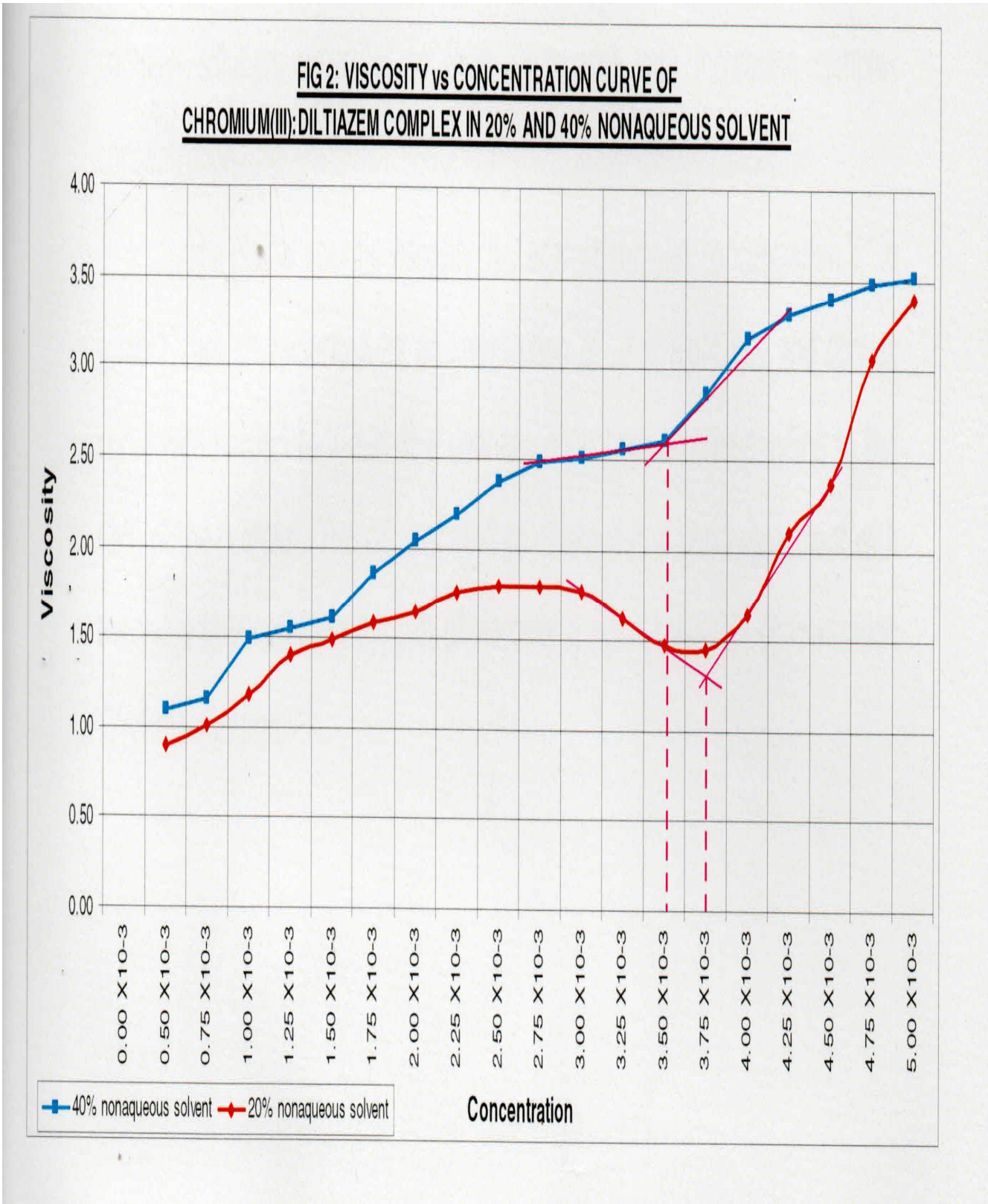

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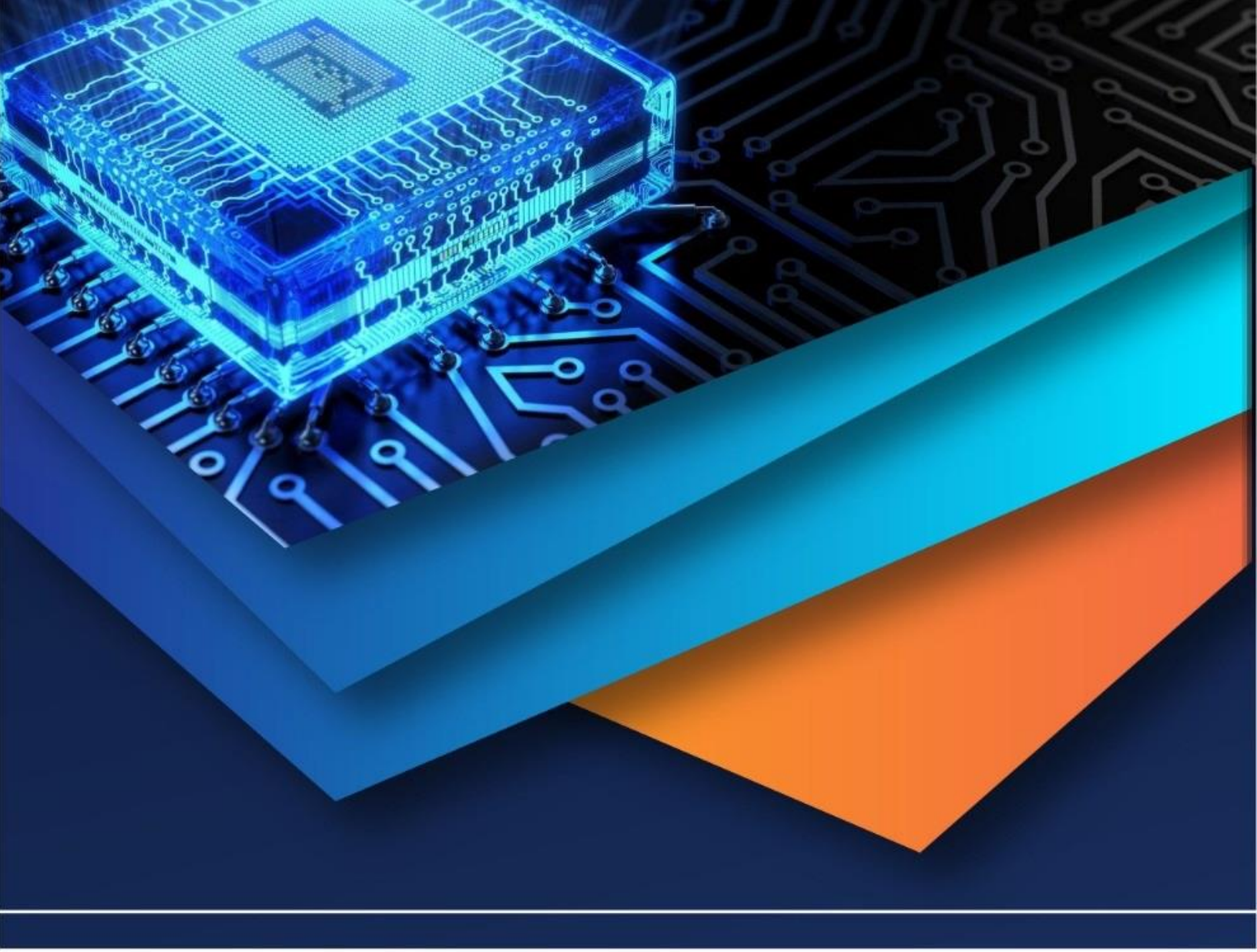

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